Mycobacterial

TB

- D.F — 1
- pathogenesis — 1
- Histopathology — 2
- classification — 2
- stages of granuloma formation — 2
- Tuberculin Test — 3
- BCG vaccine — 3
- Types of Chancre — 4
  2- warty "verrucosa"
  3- Scrofuloderma
  4- Cutis orificialis
- 5- Lupus vulgaris — 5
- 6- Tuberculous Gumma — 6
- 7- Acute miliary T.B — 6
- Immunopathology — 6
- Spectrum — 7
- Diagnosis — 7
- treatment — 8
- Tuberculids — 9
- papulonecrotic Tuberculoid — 9
- lichen scrofulosum — 10
- Erythema induratum — 10
- Atypical mycobacteria — 11
- Swimming pool granuloma — 12
- M. Ulcerans (Buruli ulcer — 13

Leprosy

- Epidemiology — 13
  Etiology
  mode of infection
  Genetic predisposit
- pathogenesis — 14
- Skin Diseases Based on TH1, TH2 — 15
- Spectrum — 16
  Classification
- leprosy in children — 17
- Types: — 18
  - Indeterminate
  Tuberculoid
  Lepromatous
  Borderline
- Histoid leprosy — 18
  Histogenesis
- HIV + leprosy — 19
  Nature of immune Deficency in LL
- Reaction leprosy — 19
- Diagnosis — 20
- Hx of leprosy — 23
- Erythema Nodosum — 25
  Erythema induratum of Bazin
- Scrofuloderma — lichen scrofulosum
- [illegible]
- [illegible]

• Cutaneous Tuberculosis •

- **Caused By**: M. Tuberculosis
  - acid - alcohol fast Bacillus
- **Exogenous exposure**:
  Produce → T.B chancre
  → T.B verrucosa Cutis
- **Endogenous infection**:
  lead to → Scrofuloderma
  → miliary T.B
  → LV

-L.V (lupus vulgaris).

- Site :- Face . Neck
- lesion • plaque "Apple Jelly" nodules → **Scar** still Contain active lesions "unhealthy scar"
- Diascopy Test :-
  pressing LV lesion è glass Slide → yellowish Brown spots "Apple Jelly"

-Tuberculids:
papulo-Necrotic - lichen Scrofulosurm - Erythema Induratum

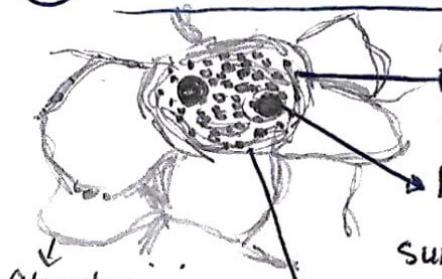
*** D.F**
- Rare Disease 1% of extra pulmonary T.B , 4% of All T.B
- Risk of infection ↑↑ By ↓↓ CMI e.g → long term ↓↓ è cytotoxics oR Steroids → lymphomas , Malnutrition

*** pathogenesis**:
- Transmitted By → **Inhalation** of infected Droplets nuclei from ptn e Active pulmonary T.B
- Cutaneous T.B → By Direct inoculation of organisms into skin By → Hematogenous Spread from an internal site of infection (Lung)
- Tuberculous Tissue Reaction triggered when : T. lymphocytes previously sensitized By M. Tuberculosis → Come in Contact with specific Tuberculous antigen
- This leads to → Activation of T. cells + **Secretion** of Cytokines → INF-γ, IL-2, TNF which attract Macrophages from circulation è **Granuloma** formation → enable them to **Kill** ingested mycobacteria → **tense** Caseous Tissue necrosis (T.B.

The **outCome** of infection depend on:
1. number + Virulence of Bacilli
2. Route of infection
3. Natural Resistance
4. Immunological Response of Host

* Histopathology:

① Tuberculous infiltrate



* Mononuclear Cells → Blood Derived Monocytes
  ↓ Develop into Macrophages → give Rise to Epithelioid cells → Some fusing → Multinucleated giant cells

② Atypical Tubercles:
- → Absence of Necrosis
- → Called "Tuberculoid infiltrate"
- → present in
  - Syphilis
  - Tuberculoid leprosy
  - Atypical MycoBacteria
  - Rosacea
  - lupus miliaris Disseminated faciei
  - F. B granuloma

* Classification of Cut. T.B:

① inoculation T.B From Exogenous Source:
- .Chancre
- Verrucosa Cutis
- lupus Vulgari's

② 2ry T.B from Endogenous Source
- Contagious spread: Scrofuloderma
- Autoinoculation on Ficial T.B

③ Hematogenous
- -lupus vulgari's
- -Acute Miliary T.B
- - T.B Gumma

④ Eruptive T.B (Tuberculoid)
- -papulo-necrotic
- -lichen Scrofulosum
- -Erythema induratum

* Stages of granuloma Formation in T.B:

1. initial stage → Expansion of Mycobacterial population in absence of adaptive immunity
   → Mycobacterial multiplication + Spread Facilitated By:
   - Formation of nascent granuloma
   - → infected Macrophages → undergo apoptosis → Recruit additional Macrophages → phagocytose Remnants of infected cells and their contents
   - → Some of These Newly infected Macrophages → Seed 2ry granuloma formation
2. → adaptive immunity occur → CD4 - CD8 effector T. cells Curtail → MycoBacterial growth

* Tuberculin Test:

- Depend on: Delayed Type Hypersensitivity to Tubercle Bacilli OR their products
- Caused By: Infiltration of skin By Sensitized lymphocytes
- The Test: applied By Intracutaneous injection of 5 PPD (5 units of purified protien Derivative) of Tuberculin Containing Tuberculoproteins (Manfoux Test)
  - → the test is read at 48-72 hrs
  - → Induration ≥ 10 mm → strongly suggest: past or present Tuberculous infection
- Tuberculin Sensitivity → appear after 3-6 weeks of onset of M. Tuberculosis infection (Life long)
- Cross Reaction may occur

* BCG Vaccine:

Bacillus Calmette Guerin → living attenuated Bovine Tubercle Bacillus used to enhance Immunity in T.B -ve

- Cut. Complications of BCG vaccine:-
  1- Specific:
    - → excessive Ulceration OR lymphadenopathy
    - → LV at site of vaccination
    - → lichen scrofulosorum
    - → papular Tuberculids – lichen nitidus
  2- Non Specific:
    - Eczema - Keloids - Urticaria - Erythema. Multi
    - Erythema nodosum
    - in AIDS pts → BCG can cause progressive mycobacteriosis
    - in ARC pts → BCG might Drive them into Terminal

* Types:

1- Iry Inoculation Chancre
2- Verrucosa Cuti's warty
3- Scrofuloderma
4- Cutis Orificialis
5- lupus Vulgaris
6- Tuberculous gumma
7- Acute miliary T.B

1	2	3	4
Iry Inoculation Chancre	**Verrucosa Cutis "warty"**	**Scrofuloderma**	**Cutis orificialis**
D.F: Rare - Result from Exogenous Direct inoculation into skin of individual **Not** previously infected - mainly children "Ghon's Focus"	Result from: Exogenous Direct inoculation into skin & individual with **High Degree immunity** e.g: accidental in physicians verruca necrogenica	Result from: Direct Extension to Skin from underlying Focus • lymph Node - Cervical, axillary • Bone • Joints - strong +ve Tuberculin	-occurin: Mucosa or skin adjoining Orifices in ptn & advanced internal T.B • pulmonary • intestinal • Autoinoculation - adult male è Bad general condition
Clinically: Site: Face or extremities lesion: Asymptomatic - Brownish Red papule OR Nodule that erode → Indurated non tender ulcer è Sharp Demarcated "undermined edges" - prominant Regional L.N Healing: Several weeks è Scar enlarged glands persist Tuberculin test −ve early +ve after 6 weeks	Site: Hands - knees - ankles lesion: Asymptomatic papule slowly evolves into **Warty** Hyperkeratotic Irregular papule → Enlarge. By peripheral extension. - Verrucous surface → Fissure from which pus expressed - **No** Regional lymphadenopathy	-lesion: Bluish - Red nodule → Breaks Down to Form **Ulcer** è Bluish undermined edges - Floor → Coverd è Soft granulation Tissue - Numerous **Sinuses** and **Fistula** present - Scarring → irregular adherent masses - Healing: puckered scar	painful shallow **ulcer** è Bluish undermined edges - rarely exceed 2cm - Healing: No tendency to heal spontaneously - Site: around mouth anus, genitalia
Histopathology: - Early: Acute non specific Neutrophilic Reaction, area of Necrosis, tubercle **Bacilli** - 3-6 wks later: infiltrate Become granulomatous è epithelioid Cells, giant Cells, lymphocytes Necrosis, sparse **Bacilli**	Marked: Hyperkeratosis Acanthosis - papillomatosis - Pseudoepitheliomatous Hyperplasia - Superficial dermal Abscess - intense mixed infiltrate è Some giant cells - Only sparse Foci - **Bacilli** → Rarely seen	Tuberculous granulation Tissue - Caseation necrosis in Deeper Tissue - **Bacilli** found occasionally	-Non specific inflammatory Reaction - Many Tubercle **Bacilli** - Prominent Caseation necrosis

4

5 Lupus Vulgaris : LV

1- D.F: most common Type.

- Start: in Childhood
- progresses → V. Slowly
- Occurin: persons è moderate or [redacted] High Degree immunity
- Tuberculin test → +++
- Site: arise at site of primary inoculation By: Direct extension from underlying infected glands OR By: Hematogenous Spread from Obscure origin

2- Clinically:

→ Site: Face, neck (90%) - Buttocks limbs

→ lesion: Sharply Demarcated Serpiginous Reddish-Brown Soft plaque

→ Composed of Deep seated nodules

→ Slow peripheral extension → leading to → thin, Contractile unhealthy scar
↓
(new lesions at area of Atrophy)

→ Scarring, Destruction of underlying structures → Nose
↳ ear Cartilage

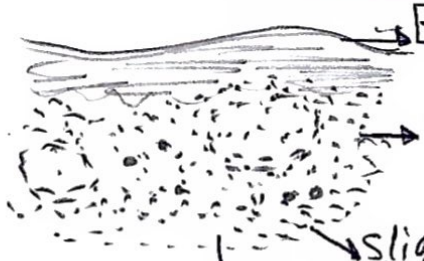
→ SCC, BCC (less comon) → Develop at the Margin

→ Mucosal involve → nasal, Buccal, conjuctiva → may occur

3- Diascopy Test:

- pressing of L.V lesion è glass slide to ↓↓ Vascularity
- Yellowish-Brown Spots " apple Jelly" nodules

4- Histopathology:



→ Epidermal changes: Atrophy - ulceration - Hypertrophy
pseudoepitheliomatous Hypertrophy

→ Epithelioid cells + Langhans giant cells embedded in Dense mononuclear cells ← lymphocytes monocytes

→ Slight or Absent of Caseation Necrosis

↓ T.B Bacilli → Difficult to Demonstrate

6 Tuberculous gumma

→ Result from: Hematogenous Dissemination From 1ry Focus During periods of Lower Resistance

→ lesion: Single OR multiple S.C Nodules → Break Down → Form undermined **Ulcer** or **Sinuses**

7 Acute miliary T.B

→ D.F: Fatal Disease affect childs and **infants** or immuno suppressed Adults

→ lesion: generalized Erythematous papules, Pustules & Ulcers

→ internal T.B → Tuberculin – ve

* Immunopathology :

- 2ry Cut T.B forms a Continous immuno pathologic spectrum → Extending from **LV** through **TVC** and **SF** to **TCO**

- **LV** → Represent the "High immune" pole with Active CMI and Normal humoral immunity
- **SF + TCO** → Represent "Impaired CMI" pole & predominantly humoral immune Response
- **LV** granuloma (active CMI) → lymphocytic preponderance
  - → absent or scanty T.B Bacilli
  - → absent / slight Caseation Necrosis
- **SF + TCO** (Impaired local immunity) →
  - relative depletion of lymphocytes
  - frequent giant cells & many Bacilli
  - Regular presence of Caseation necrosis

* Spectrum of Cut. T.B :- جدول

The spectrum of cutaneous TB ②

	LV	TVC	SF	TCO	Miliary TB	TB chancre	Tuberculids
Mode of infection	Inoc./Hemat.	Inoc.	Contig. spread	Autoinoc.	Hemat.	Inoc.	Hemat.
Tuberculin	+++		++	±	-	- → +	++
AF bacilli	±		++	+++	+++	+++ → ++	-
Caseation necrosis	±		++	+++	+++	+++ → ++	++

*Diagnosis:

1- Tuberculin skintest

2- IFN-γ Release assays: (QuantiFERON T.B Gold), T-SPOT)

These assay → Determine if exposure to Recombinant peptides from M. Tuberculosis

Stimulate IFN-γ production By T. Cells within ptn Blood Sample

ESAT.6
TB7.7
CFP-10

- this assay has great specificity and similar sensitivity Compared to Tuberculin skin tests.
- may Be used in place of Tuberculin skin test in all situations
- Tuberculin skin Test → preferred in children < 5 yrs
- IFN γ relase assay → prefered in ptns

★ groups that historically have Low Rates of Returning for 2nd visits

e.g → homeless
→ Drug users

★ individuals who have Received BCG

*A Diagnosis of TB Cutis:

Absolute Criteria

1- +ve culture on lewenstein Jensen's media from lesion

2- Guinea pig inoculation

Relative "unreliable" Criteria:

1- clinical history, signs
2- presence of Active proven TB Focus elsewhere in Body
3- presence of acid-fast Bacilli in lesion its self
4- Histopathology
5- +ve reaction to tuberculin
6- Effect of specific therapy

→ Multibacillary : → pauci bacillary

1- Tubercules chancre
2- Scrofuloderma
3- Tuberculosis orificialis
4- Acute miliary T.B
5- Gumma T.B

1- Tuberculosis Verrucosa Cutis
2- Lupus vulgaris
3- Tuberculoids

* treatment:

(*) Drugs :- All Drugs on empty stomach once daily

Isoniazid (INH)
- 300 mg/Daily Adults
- Orally /6 mnth

Rifampicin
- < 50 kg = 450 mg
- > 50 kg = 600 mg

Daily oral /6m

pyrazinamide
- For the 1st 2 months
- < 50 kg = 1.5 g
- 50 - 75 kg = 2 g

Ethambutol
- for first 2 months
- 15 mg/Kg
- Daily

(*) Drug Regimens :

Initial phase
- For 2-3 months
- using at least
  - 3 Drugs → INH, Rifampicin, Ethambutol
  - 4 Drugs → INH, Rifampcin, pyrazinamide, either Ethambutol or streptomycin

Continuation phase
- For several months
- using 2 Drugs only
  - INH
  - Rifampicin

*HIV-infected ptns
- as HIV -ve But Dose adjustments necessary
- Should avoid Rifampin in ptns who are on protease inhibitors

8

*Ptns Receive pyrazinamide should undergo : Baseline and periodic Serum Uric Acid assessments

*Ptn Receiving Long term Ethambutol Should undergo Baseline and periodic Visual Acuity and Red.green color Precipitation Test

*Calciferol vit D2 , 150000 U For 5 Days a week

Toxic Dose For LV

→ acting on the tissue Not the Bacilli
→ promoting fibroblasting proliferation and strangling the tubercles

*Surgical treatment:
→ excision of small lesions of LV or Warty T.B
→ plastic surgery for mutilation and Deformity

*Pregnant women's Active T.B
→ Should Be treated even in first stage of pregnancy
- INH - Rifampcin - Ethambutol - pyrazina -
- Streptomycin Should Not used

*MultiDrug-Resistant TB MDR-TB

1- Resistant to INH and Rifampcin [the most two effective]
2- 4% of all new T.B Cases
3- when MDR-TB → start tt empirically Before Culture Results Become available Then modify the Regimen as necessary
4- Never add a single new Drug to failing Regimen
- Administer at least 3 (prefer 4-5) of following medications:
  1- Aminglycoside: Streptomycins, Amikacin, kanamycin
  2. Fluoroquinolone: Levofloxacin, Ciprofloxacin, Ofloxacin
  3- thioamide: Ethionamide, Prothionamide
  4- Pyrazinamide
  5- Ethambutol
  6- para-aminosalicylic acid
  7- Rifabutin

*Extensively Drug-Resistant tuberculosis:

1. Resistant to INH and Rifampin
2. Resistant to quinolones → the most effectie 2nd line Drugs
3- Resistant to at least one of three injectable 2nd-line Drugs: - Amikacin - Capreomycin - kanamycin

Tuberculids

- Result from: Hematogenous Dissemination of tubercle Bacilli → from Distant source
- leading to: Delayed type hypersensitivity Response in peisons e High Degree of CMI
- The original TB Focus: Not active at time of Eruption
- The Bacilli → Absent from the lesion
- The lesion: → Bilateral - Symmetrical - in Crops with tendency to spontaneous healing

(Rosacea-like tuberculid) (Lupus miliaris Disseminatis Faciei)
↳ No Longer Cosidered as Tuberculoid

Critria of Diagnosis: • +ve tuberculin test • Evidence of TB elswhere • Tuberculoid granuloma in histology • good Response to Drugs

Classes and activities of anti-tuberculous agents HL

The agent	Spectrum of activity
1st line agents	
Rifampin	Broad
Isoniazid	Tubercle bacilli
Pyrazinamide	Tubercle bacilli
Ethambutol	Tubercle bacilli
Rifapentine	Broad
Rifabutin	Broad
2nd line agents	
Kanamycin, amikacin, streptomycin	Broad
Capreomycin, viomycin	Broad
Levofloxacin, ofloxacin, moxifloxacin, gatifloxacin	Broad
Ethionamide, prothionamide	Tubercle bacilli
Cycloserine, terizidone	Broad
Para-aminosalicylic acid	Tubercle bacilli
3rd line agents	
Clofazimine	Mycobacteria
Amoxicillin/clavulonate	Broad
Linezolid	Broad
Imipenem	Broad
Thiacetazone	Tubercle bacilli
Clarithromycin	Broad

* papulonecrotic tuberculids *

- Lesion: Recurring Symmetrical crops of non-itchy - Dusky Red papules on
- extensor surface of extremities
- Face, ears, Buttocks

↓

undergo Central Necrosis

Heal è pigmented pitted scars -

- Histopathology:
- Early: leukocytoclastic Vasculitis
- later: wedge shape Necrosis è the Base toward the epidermis and perivascular mononuclear infiltrate

↓

wedge → extruded out → Epithelioid and giant cells → appear at periphery

* lichen scrofulosorum *

- D.F: Grouped - closely set, minute lichenoid, slight Scaly, Reddish Brown - perifollicular papules
- Site: Trunk. heal without scarring

- Histopathology:
  - superficial Dermal granulomata → Surround follicles and sweat Ducts
  - composed of → Epithelioid cells
    - → some Langhans giant Cells
    - → narrow margin of lymphoid cells at periphery
    - → No Caseation
  - +ve PCR DNA

* Erythema induratum " Bazin " *

→ Women more specially è T.B and acrocyanosis

→ Clinically: → persistant, Recurrent → tender nodules on the Back of Lower legs → (Calves)

↓

progress to Ulceration

→ The Ulcer: irregular - Shallow with Bluish undermined edges

→ Healing: with atrophic scars Recurrence: Common

PE: onset of Cold

→ Histopathology:

- Epithelioid Cell tubercles in Deep Dermis
- proliferation of walls of Blood vessels and invasion of their walls By inflammatory infiltrate

" Vasculitis " → Endothelial Swelling + Thrombosis of lumen

Cutaneous tuberculosis*

Disease	Clinical findings	Immunity / Route
Scrofuloderma	Deep nodule typically over cervical lymph node → turns fluctuant & suppurative → ulcerates Heals with prominent scarring	***Immunity:*** sensitized host (low immunity) ***Route:*** contiguous spread (from underlying lymphadenitis)
Tuberculous chancre	Painless red-brown papule at inoculation site → non-healing, non-tender undermined ulcer with painless regional lymphadenopathy	***Immunity:*** non-sensitized (no prior immunity) ***Route:*** exogenous (direct inoculation); primary infection
Tuberculosis verrucosa cutis (warty TB)	Small indurated hyperkeratotic papule over hand, ankle, or buttock → warty plaque with serpiginous borders Spontaneous resolution with scarring	***Immunity:*** sensitized host (moderate to high immunity) ***Route:*** exogenous (direct inoculation at site of trauma); reinfection
Lupus vulgaris	Gelatinous reddish-brown nodules involving face or neck with brown-yellow color ("apple-jelly") on diascopy	***Immunity:*** sensitized host (moderate to high immunity) ***Route:*** hematogenous, lymphatic or contiguous
Tuberculosis cutis orificialis	Painful erythematous papule → ulcerates with undermined borders; typically in oral cavity (but can also be genitourinary)	***Immunity:*** sensitized host (impaired cellular immunity) ***Route:*** autoinoculation from underlying visceral infection
Miliary tuberculosis	Tiny bluish-red papules (teeming with bacilli) which become crusted; seen mainly in infants or immunosuppressed patients	***Immunity:*** nonsensitized (low immunity) ***Route:*** hematogenous dissemination
Tuberculous gumma	Firm, deep seated nodule over trunk, face or extremities → turns soft & fluctuant → ± ulceration	***Immunity:*** immunosuppressed host ***Route:*** hematogenous
Papulonecrotic tuberculid	Dusky erythematous papule central necrosis & crust formation	***Immunity:*** sensitized ***Route:*** hypersensitivity reaction to distant focus of TB (tuberculid)
Lichen scrofulosorum	Lichenoid tiny papules (tuberculids)	
Erythema induration (Bazin disease)	Subcutaneous inflammatory nodules with ulceration on posterior calves	Associated with past or active TB

** Adapted from: Dermatology, illustrated study guide & comprehensive board review, 2012.*

* ATypical MycoBacteria *

(NTM) non tuberculous

- exist → free in the environment (water, soil)
- M. Tuberculosis , M. leprae → always pathogenic But ATypical mycoBactria have Low Degree of virulence
- PF → is necessary to produce infection (obstructive pulmonary Disease, Trauma, HIV)
- they enter human Body By : inhalation, skin Trauma
- unlike T.B → infection with these organisms is acquired from Environment Not From human source

49 جزء

Clinical manifestations of non-tuberculous mycobacteria (NTM) [2]

Clinical manifestations	Common species
1. Chronic pulmonary disease in adults: the most common type of infection	MAC* & M. kansasii
2. Superficial lymphadenitis "mainly cervical": the most common manifestation in children	MAC & M. scrofulaceum
3. Disseminated disease in immunosuppressed patients, e.g. AIDS, lymphomas, cytotoxic drugs, ... etc.	MAC**, M. kansasii & M. hemophilum
4. Cutaneous manifestation: usually produced by inoculation or by dissemination from a distant focus: • Swimming pool granuloma & its sporotrichoid variant. • Buruli ulcer. • Subcutaneous nodules, abscesses, plaques & cellulitis-like.	 M. marinum M. ulcerans M. kansasii, M. fortuitum / chelonae, MAC

* MAC = M. avium complex consists of 2 species: M. avium & M. intracellulare

* Swimming pool granuloma *

- **Dif:** granulomatous Reaction in skin
- Due to: infection è *M. marinum*
- Aquired infection: through minor abrasions occur while Bathing in insufficiently chlorinated swimming pools
  - more commonly From: Home aquariums "fish tanks" → where the organism is Naturally present

- **Clinical:-**
  - 2-3 weeks after inoculation
  - lesion: Solitary Dusky-Red papule OR nodule
  - site: mainly: fingers, knees, elbow feet
  - → Slowly Enlarges into Verrucous plaques
  - → Superficial ulceration occur
  - → "**Sporotrichoid** form" may occur with Nodular or ulcerating lesions Along line of: Lymphatic Drainage
  - → Healing: Spontaneously within 1-3yr

- **Diagnosis:**

1- **Histopathology** → Early lesions < 6 months:-
non-specific inflammatory infiltrate
→ in older lesion: > 6 months:
well formed tuberculoid granulomata with Fibrinoid Necrosis Rather than True Caseations
→ Langhans giant cells → ocassionaly seen
→ Intracellular acid fast Bacilli (Longer and Broader than M. Tuberculosis) → rarely seen

2- **Culture** → +ve in 70% of Cases

3- **Tuberculin test** → +ve But è little Value

- **Treatment:**

Clarithromycin - Minocycline - Rifampin
Ethambutol - Trimethoprim - Sulfamethoxazole

- 2 agents for serious infection → Clarithromycin + rifampin or Ethambutol
- Combination of rifampicin and Ethambutol OR minocycline OR Trimoxazole OR clarithromycin OR Azithromycin

* Infectious Causes of lymphocutaneous "Sporotrichoid" pattern:

1- Atypical mycobacteria "M. mainum
2- Sportrichosis 3- Nocardiosis
4- pyogenic Bacteria (S. aureus)
5- leishmaniasis 6- Tularemia
7- Tuberculosis 8- Dimorphic fungi
9- opportunistic fungi: Fusarium

* M. Ulcerans "Buruli Ulcer"

- D.f: unusual among myces Baeteria → produce a toxin (mycolactone) → Responsible for clinical manifistations
- its Aquired → mainly children, after minor Trauma with an average incubation period of 2 months

- Clinically:
  - Itchy . S.C . Firm . Nodule
  - Site: mainly on Legs or forearm
  - Break Down to Form → rapidly extending, painless Shallow necrotic Ulcer & undermined edges Base of necrotic Fat
  - Healing: after few months with prominent scar and Contracture formation

- Diagnosis: from Travel History to tropical endemic area
  1. Histopathology: granulomatous process with Considerable S.C Fat necrosis
     - Clumps of AFB seen in Center of lesion
  2. Biobsy: from edge of ulcer, numerous extracellular AFB
  3. Burulin Skin test: Little Diagnostic

- treatment:
  1- surgical excision & grafting
  2- For extensive Disease: combination of rifampicin + cotrimoxazole + minocycline
     OR Rifampcin + Streptomycin → 4 weeks
  3- Localized Heat Therapy (M. ulceran prefer Cooler temprature)

•Leprosy•

1-Epidemiology:

- more in tropical, Subtropicals areas → Africa, South East Asia, Latin America
- ↓↓ numbers after MDT
- occur in all age groups with Average 10-20 yrs
- Children at great Risk

2-Etiology:

→ Caused By: Mycobacterium Leprae
↓
obligate intracellular parasite

- Stained By: Ziehl-Neelsen as it's Acid Fast Bacillus
- its Dosn't grow in usual media
- Can be inoculated in mice foot Pads and in nine Banded armadillo
- M.leprae → Multiplies Slowly → So leprosy Develop slowly months and years

- Structure: Straight Rod 1-8 µm

2 main lipids:
1. phthiocerol Dimycocerosate — shared By other mycobacteria
2. phenolic glycolipid PGL-1 — Specific for M.lepra

3-mode of infection: IP = 2-7 yrs

→ occur through → prolonged **close Contact** of suspected individual with an open Case of leprosy (untreated pts è multibacillary leprosy è +ve nasal scraping)

→ Infection occur through:
- Insect-Bites ↔ Droplet air-Borne infection
- Feco-oral route ↔ Contact è Ulcerated lesions
- Blood borne

→ Can transmitted through milk of lactating mothers

4-Genetic predisposition:

1- familial Clustering of Cases
2- High Concordance rates in identical twins
3- associated of HLA-DR2-DR3 with TT. HLA-DQ1 è LL

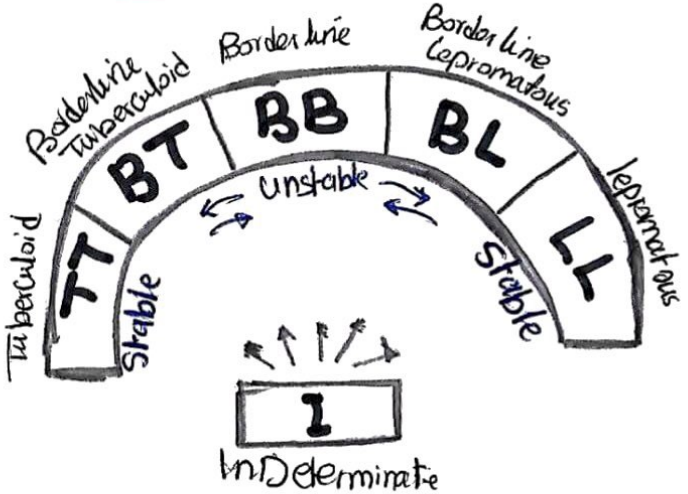
5- Pathogenesis + classification:

1. most People Develop "Subclinical infection" and Recover Naturally
2. Few people who Develop "the Disease"
3. The Target is "Neural tissue"
   Shwann cell → which engulf the Bacill. and the type of leprosy ocur Depend on the Degree of Cell mediated immunty (CMI - Tcells) of infected ptn.
4. Stimulated T-Cells → Secrete lymphokines which activate Macrophage to Digest M. Leprae
5. eliminate the Bacilli is made By: Macrophages
   when in Contact ẽ M. leprae → ↑ production of Cytokines (IL-1, TNF, IL-12) → These Cytokines stimulate The number and activity of Macrophages
6. prediminantly Th1 CD4 T Cell Response seen in ptn (TT) → producing IL-2 - IFN and TNF → Thant maintain the inflammation
7. in (LL) → a predeominantly Th2 response → Leads to Release of IL-4 - IL-10 - IL-5 - IL-13 That suppress Macrophage activity
8. the number of T Cells:
   - ↳ maximum number present in TT
   - ↳ Decline in number across leprosy Spectum
   - ↳ LL → only Few lymphocytes are seen
9. CD4 Cells and CD8 Cells:
   - ↳ CD4 Cells ↓↓ while that of CD8 Cells ↑↑ from tuberculoid to lepromatous end
   - ↳ CD4 : CD8 ratio is higher in TT

6- Skin Diseases Based on Th1 - Th2

Th1 - Dominant skin D	Th2 Dominant skin Diseas
- Tuberculoid leprosy	- Lepromatous leprosy
- Localized leishmaniasis	- Disseminated leishmaniasis
- Allergic Contact Dematitis	- Acute atopic Dermatitis
- lichen planus	
- Early (patch-plaque) CTCL	- Advanced CTCL / Sezary S
- psoriasis	
- Acute GVHD	- Chronic GVHD

7. Spectrum of leprosy:



- 5 Types of leprosy occur forming spectrum
  - → One pole → Tuberculoid leprosy **TT** occur in persons è Very High Degree immunity
  - → Followed By **BT**, **BB**, **BL**
  - → one the other end of spectrum is Lepromatous leprosy **LL** occur in persons with Very Low Immunity
  - → **Intermediate** leprosy is the initial manifistation of leprosy in ptn è **Undeterminate** immunity
  - → only the two polar form → **Stable** while all other → **Unstable**

8- Classification:

① Ridley-Jopling system
- → Depend on host Response to organism
- - TT - BT - BB - BL - LL

② WHO system:
- → according to number of lesions
- → and presence of Bacilli on skin Smear into :-

Paucibacillary leprosy
- 5 or fewer lesion è absence of organisms on smears
- - Tuberculoid - Borderline Tuberculoid Leprosy From Ridley-Jopling system

Multibacillary leprosy
- 6 or more lesions è possible visualization of Bacilli on smear
- - Lepromatous leprosy - Borderline lepromatous leprosy, mid Borderline leprosy on Ridley-J. system

9- Leprosy in children:

1- Infants, young children → High risk group in families of infective leprosy ptns → Because of great chance of exposure

2- Mode of infection
- → Abrasions, ulcers,
- → Transplacental transmission
- → mothers milk

3- clinically:
- → Non lepromatous "paucibacillary" leprosy :- leprosy predominates
- → lepromatous "multibacillary" forms : Uncommon in children

5- Healing: 75% of children è leprosy → Complete Remission in few months without ttt

Indeterminate	Tuberculoid	Lepromatous	Borderline
D.F Early Transitory stage • typically seen in: Children ch.ch By:	Developing persons è good immunity → prevent Dissemination of Bacilli → Early Destruction of nerve fibers → Few well defined lesions → absent Bacilli	- Developing: persons è **Low** CMI	- Immunologically **Unstable** - evolve towards: **LL** → without ttt **TT** → with ttt
Clinically Single-Few • Hypochromic - Erythematous **Macules** - Normal Sensation	• **Skin**: Single-few. Asymmetric Erythematous - Hypopigmented **patches**, è well-defined elevated **Border**, tendency to **Central** clearing **Surface** → Dry. anhidrotic. hairless è Early Hypoesthesia • **peripheral nerves**: Early → involve **TT** → wasting paralysis of small muscles of **Hand** and **feet**, anesthesia of limbs trophic changes - The sensation lost in Following: **Heat** Then **Pain** Then touch - The involved nerve: thickened Nodular - Tender - some Cases limited to peripheral nerves only " **Neural Type**: → **Affected** nerves: 1- Ulnar 2- Great auricular 3- posterior tibial	- **Early**: Skin, mucosa - **Late**: neural - Systemic • **Skin**: numerous - Bilateral Symmetrical, 3 types ↳ 1- **Macular**: numerous - ill defined. Erythematous Hypopigmented Macules ↳ 2- **Nodular**: skin-colored - pink Copery papules - Nodules - Smooth, Shiny overlying skin - Sensory changes → slight - absent - Early nodules → on Face (ears) ↳ any part except warmest parts - Face " **Leonine** apperance " - The outer third eyeBrows Lost - Ichthyosis in Lower Limbs ↳ 3- **Lucio**: Diffuse infiltration of Skin **without** Nodules è Alopecia of eyeBrows + Eyelashes	**Skin: BT** lesion Similar to TT But Smaller - more numerous - less sharply Demarcated - Small satellite lesion - Nerve → slight enlarge **BB** - numerous Red plaques ill-defined sloping external edges in **LL** - well-defined central Punched out Space of normal skin in **TT** " Swiss-cheese appearance **BL** - as in LL: numerous macules, papules Not symmetrical - **No** Lepromatous features (Leonine madarosis)

Indeterminate	Tuberculoid	Lepromatous	Borderline
Polarity: ① if lymphocytes: numerous aggregated around the Nerve → lesion Dosn't Resolve → will Develop **TT** ② lymphocytes: Scanty ~ Bacilli Condemonstrated lesion → progress to **LL**	-optic nerve **Not** affected Dute Absence of schwann sheath	• **Nerve Damage**: late (after 3-4yrs) in Bilateral pattern → anesthesia - muscle paralysis trophic changes • **Mucous membrane**: URT ∈ repeated attacks of Epistaxis • **organs**: liver · spleen · L.N · muscle	
Histopathology: Non-specific Inflammatory infiltrate	-Epithelioid Cells granulomas (elongated as they follow nerves) ∈ slight admixture of → monocytes → giant cells → slight caseal necrosis - Lepra Bacilli → Absent	- The **infiltrate** separated from flatened epidemis By:- narrow zone of nomal Collagen - The **infiltrate** Composed of:- ★ Macrophages ★ abundant foamy Cytoplasm - Lepra Bacilli → Large numbers in Bundles	mixtures of lepromatous and tuberculoid changes
Bacteriology: Few or No Bacilli	lepra Bacilli **Absent** in skin lesion	lepra Bacilli **Present** in Large number in skin + Nasal smears	lepra Bacilli Can Be Demonstrated But **Fewer** than LL
Immunologically: **Clepromin test:** Variable Response	lepromin test strongly **+ve** indicating → High Degree of **CMI**	**-ve** lepromin test (Absent CMI) Anti-bodies to M. leprae antigens Detected in high titre - many **Autoantibodies** are produced Including: Antinuclear · anti-Thyroid antisyphilic Reagents - **Antibodies** in Leprosy Don't have any protective Role → unable to get at the intracellular organism	weak + ve OR Weak - ve

scale are included in the

Clinical findings	LL	BL	BB	BT	TT	I
Type of lesions	Macules, papules, nodules, diffuse infiltration	Macules, papules, plaques, infiltration	Plaques & dome-shaped, punched-out lesions	Infiltrated plaques	Infiltrated plaques, often hypo-pigmented	Macules, often hypopigmented
Number of lesions	Numerous	Many	Many	Single, usually with satellite lesions, to more than 5	One or few (up to 5)	One or few
Distribution	Symmetric	Tendency to symmetry	Evident asymmetry	Asymmetric	Localized, asymmetric	Variable
Definition	Vague, difficult to distinguish normal versus affected skin	Less well-defined borders	Less well-defined borders	Well-defined, sharp borders	Well-defined, sharp borders	Not always defined
Sensation	Not affected	Diminished	Diminished	Absent	Absent	Impaired
Bacilli in skin lesions	Many (globi)	Many	Many	Few (1+), if any, detected	None detected	Usually none detected

LL, lepromatous leprosy; BL, borderline lepromatous leprosy; BB, mid-borderline leprosy;

	Tuberculoid (TT)	Borderline (BB)	Lepromatous (LL)
Skin lesions	Single or few, asymmetrical, well-defined erythematous or hypopig. patches, with hypoesthesia, hair loss & anhidrosis & tendency towards central clearing.	Few or several asymmetrical, erythematous, partly well-defined patches, annular & punched-out lesions are characteristic.	Numerous, symmetrical distributed, erythematous or shiny ill-defined macules, papules or nodules. glistening There may be leonine face, loss of eye brows & eye lashes.
Sensory impairment	Marked	Marked in BT, slight in BL	None in early lesions
Peripheral nerves	Single (related to the lesion), enlarged, hard & tender. The condition may be limited to peripheral nerves (neural type).	Several asymmetrically affected.	Many, symmetrically affected, late onset → anesthesia & muscle wasting.
Bacteriology (skin smear)	-ve	Usually +ve	Always +ve
Internal	- ve	- ve	+ve
Lepromin test	Strongly +ve	Weakly +ve (in BT), - ve (in BL).	Always –ve
Skin biopsy	Tubercles of lymphocytes, epithelioid cells & Langhans giant cells in dermis without AFB.	Mixture of tuberculoid & lepromatous features.	Diffuse, spindle-shaped macrophages, foam cells with subepidermal free clear zone.
Course & prognosis	Relatively benign & stable with good prognosis	Unstable may progress to subpolar types, with variable prognosis. Prone to type I reaction.	Most infectious with poor prognosis prone to type II (ENL) reaction.

10 - Histoid leprosy : (lepromatous)

- Distinct form of multibacillary leprosy
- with ch.ch { clinical, Bacteriological, Histopathological feature }
- may arise Denove or as a relapse after inadequate leprosy tt
- its tt as: multibacillary Form

11 - Histogenesis of pathological Features :

TT	Contrast	LL
- Macrophages Digest The shwann cells ê The Bacilli → Epithelioid Cells which are free of mycobacteria and contain No lipid		- Macrophages Unable to Digest Baeilli adequetely → Macrophages ê foamy apperance D.t → presence of greatly enlarged phagocytic Vacules filled ê lipid → Derived from the waxy Coat of the Mycobacteria - large number of lepra Bacilli → Present in Macrophages

12 - HIV infection and leprosy :

* The effect of HIV infection D.t ↓↓ CMI on leprosy:
  1. Conversion of subclinical to Overt leprosy
  2. Induction of Downgrading
  3. Adverse effect on chemotherapy
  4. promotion of complicating ENL

13 - Nature of immune deficency in Lepromatous leprosy :-

① **Suppressor cell Hypothesis** :-
(M.leprae-induced suppressor T.lymphocytes) → are present in peripheral Blood of Lepromatous leprosy ptn But Not in that of Tuberculoid ptns

② **Clonal Deletion hypothesis**
(TH cells Reactive to M.leprae) → are defective in Lepromatous leprosy → lead to → inadequate production of IL-2, IFNX and othe lymphokines
- Macrophages → aren't activated and unable to Digest M.leprae

③ **Role of Macrophages**:
Lepromatous Macrophages defective in (expressing cell Surface markers) activating IL-2 → in Relasing the T-cell

14 - Reactions in leprosy :

- D.f: During the chronic course of leprosy
  - → Acute episodes (Reactions) may occur.
    - may occur → spontaneously
      or
      → precipitated By :
        - effective tt
        - intercurrent infections
        - injury
        - physical stress
        - surgical operations
        - pregnancy
        - vaccination against (- Small Box, HIV)

Type I	Type II Erythema Nodosum Leprosum	type III Lucio phenomenon
Lepromin ↑ Response in Reversal state ↓ Response in Downgrading state	No effect	
pathogenesis • changes in CMI • Comprises upgrading + Downgrading	Immune Complexes → Cutaneous + Systemic small vessel Vasculitis	- in ptn who have Recived No or inadequate tt - Dense aggregate of Acid fast Bacilli
Type of leprosy • mostly **Borderline**	mostly **LL + BL**	• exclusive in Diffuse **Lepromatous L**
Clinicaly • Abrupt onset è Erythematous and edematous changes in **Old** lesions • Tenderness + swelling of **nerves**	• Acute onset of • Fever • malaise • arthralgia • Bilateral + Symmetrical Erythematous tender Nodules on Face + extensors	- Fever - tenderness - leukocytosis ✗ Abscent - lisen limited to Lower extremities, Buttocks, forearm - palpable - Hgic - sharply marginated irregular **plaque** → Crusts → Ulcer
Histopathology • shift toward Tuberculoid pole in : Reversal Reactions • shift toward Lepromatous pole in : Downgrading Reaction 19	• Neutrophilic - leukocytoclastic Vasculitis • Scanty Fragmented Bacilli around vessels	• Vascular changes → prominant • Endothelial proliferations → luminal Obliteration • Thrombosis of medium vessels • Sparse mononuclear infiltrate

15- Diagnosis:

1 Slit Skin Smear:

- site: from suspected lesions or sites commonly affected in LL ← ear lobes, forhead, chin, Dorsa of fingers

↓

- Tequnique:

1- The lesion → cleaned e' alcohol
2- a fold is picked-up Between Thumb and forefinger
3- Squeezed tightly to Render it free of Blood
4- Small incision made into dermis (5 mm Long - 3 mm deep)
5- The Blade then turned at right angles to Cut → used to Scrap The Cut surface of Tissue.
6- Fluid → obtained is Smeared onto a Slide + allowed to Dry (Blood smear is useless)
7- Then fixed over a flame and Stained By "modified ZN method"
8- Bacilli are seen as Red Rods against Blue Background.

* Bacterial index BI: = Density of Bacilli in smear

→ helpful in → Classification of leprosy
→ in Advanced LL → BI = 5+ or 6+
→ the index ↓↓ across the spectrum → 0-2+ in BT leprosy
→ Slit skin smear are -Ve in TT
→ under treatment: Bacilli Disappear from BB lesions in mnths
→ The last +Ve site are: Dorsa of fingers
From BL lesion in 1-2 yrs
From LL lesion in 6-10 yrs

* Morphological index MI: = percentage of solid staining Bacilli

→ These are Living Bacilli
→ the fragmented and granular Bacilli are Dead
→ its useful index of progres under treatment
→ in LL → MI reach Zero in 4-6 weeks on MDT

Grading of BI

6+ => 1000 Bacilli
5+ = 100 - 1000
4+ = 10 - 100
3+ = 1 - 10
2+ = 1 - 10 Bacilli/100 FF

Diagnosis in edemic Countries:

→ Clinically 2 out of 3:
1- Anasethsia → in skin lesion or in peripheral nerve Distrubution or over Dorsal Hands + Feets
2- Thickened nerves (at site)
3- Typical skin lesions
4- By prescence of Acid Fast Bacilli in Slit skin smear.

2 Nasal Scrape:

→ to Detect → open Case
→ Bacilli in nasal mucosa → granular and Disappear in much shorter time
→ Examination of Nasal mucosa may also Done

3 Skin Biobsy :-

- (Deep Biobsy to S.C Fat necessary)
- The Bacilli in leprosy Can be detected By:
  1- Gram, Ziehl Neelsen, Fite, Wade stain → all stain Bacilli Bright Red
  2. Sudan III + Sudan IV "Scarlet Red Stain → Stain Bacill Black and Red → Respectively
  3. Methenamine silver Stain → Detecting fragmented acid fast Bacilli
  6. 6 sections Be examined in lesions where Bacilli are scanty → to Be Sure Declering them -ve

4 Nerve Biobsy:

5 Lepromin test:

- "Lepromin" is Crude - Semi standardized preparation of Bacilli from a lepromatous nodule (or infected armadillo liver
- non-specific (not Diagnostic) test
- it's Strongly +ve in TT, weakly +ve in BT -ve in BB, BL, LL, unpredictable in indeterminate
- mechanism:
  - 0.1 ml of lepromin → injected intradermally
  - The site is examined after 48 hrs "Fernandez reaction" or 3-4 weeks → "Mistuda reaction"

+ve Fernandez
- indicate Delayed Hypersenstivity to antigens of M. leprae OR Cross reacting reaching mycobacterium

+ve Mistsuda
- indicate that the person is Capable of mounting an efficient CMR to M. leprae
- ē prognostic value
- negativity → can Be used as prognostic index to identify People at Risk
- pt ne LL → never Become lepromin +ve even if healed

- Interpretation of mitsuda reaction: →
  - Nothing = -ve
  - ≤ 3 mm papule ± dobtful
  - 4-6 mm papule = +ve
  - 7-10 mm papule = ++
  - > 10 mm nodule or ulceration irrespective of size = +++

6- Histamine test:

- its Detect the Damage Done to Dermal nerves in Leprosy
- a drop of sulphate of Histamine
- applied to Hypochromic Macule and another elsewhere as Control
- as the underlying area is Scarified
- The Control area → show triple Response
  → Erythema replaced By a wheal → which later surrounded By large Erythematous Flare
- in Leprosy especially in tuberculoid there is No flare.
  in Borderline & indeterminate → the flare is weak + Develop late

7- Pilocarpine test:

- Tincture of iodine → applied to the suspect lesion
  + Normal Skin as a control
- prior to injection of pilocarpine into these sites
- Then These area are Dusted è Starch powder → will Turn BLue → if there is Normal Sweating
- its ↓↓ in lesions of leprosy → as sweating depend on the integrity of parasympathetic nerve fibers.

8- SeroDiagnosis:

1- antibodies to M.lepra antigens < Highest in LL / Lowest in TT

2- ELISA: "Enzyme-Linked Immunosorbent Assay"
For antibodies against phenolic glycolipid:
- useful Screening test
  ↓↓ During chemotherapy
  ↓ Higher in LL, BL
  ↓ Lower in TT

3- FLA-Abs
"Fluorescent Leprosy Antibody Absorption test"
- For detection of M.leprae Specific antibodies

4- RIA: "radioimmuno assay"
- For antibodies to Cell-wall antigen 7 of M.lepra

5- PCR: For Detection of M.lepra DNA

16-Treatment of Leprosy:

① chemotherapy:

Dapsone
- the most important Drug + Cheapest
- Daily adult Dose 100 mg

Rifampicin
- The most potent Bactericidal anti-leprosy
- oral Daily Dose 600 mg ½hr Before food

Clofazimine "Lamprene"
- effective as dapsone
- Mainly Bacteriostatic
- Has anti-inflammatory effect
- Daily oral Dose 50 mg è meals orè glass of milk

Isoprodian:
= INH: 175 mg + Prothionamide: 175 mg + Dapsone: 50 mg

→ 15-30 kg = 1 tab/day
→ 30-50 kg = 2 tab/Day
> 50 kg = 4 tab/day

2nd generation multiDrug therapy
- Minocycline = 100 mg/day → for multibacillary ptn/3 months ↓ killing all viable M. lepra e
- Clarithromycin = 500 mg/Day
- Fluroquinolone (pefloxacin, ofloxacin) = 400 mg/day/22 days → killing 99.99% of viable M. lepra in multibacilly

Single Drug Combination
- (Rifampicin + ofloxacin + minocycline)
- tried For ptn è single skin lesion
- also WHO recommended for paucibacillary leprosy è single skin lesion

-MultiDrug therapy Regimens MDT
in adults: → I paucibacillary leprosy (I-TT-BT)
- Daily • atHome → Dapsone 100 mg
- monthy • undersupervision → Rifampicin 600 mg
- Duration = 6 months

→ Multibacillary (BB-BL-LL)
- Daily • at Home → Dapsone 100 mg + Clofazimine 50 mg
- monthly • undersupervision → Rifampicin 600 mg + Clofazimine 300 mg
- Duration = 2yr → until -ve

for single paucibacillary
single dose
- Rifampicin 600 mg
- Ofloxacin 400 mg
- minocyclin 100 m

II Treatment of reactions:

- Precipited Factors: ← Immunization, pregnancy, intercurrent infection
  Should avoided
- Chemotherapy → Continued as usual
- Mild Reactions →

Aspirin 600 mg / 4-6 hrs
Chloroquine 150 mg / 8 hr

Type II

- **Thalidomide 400 mg**
  - at night
  - Never to women in child-bearing period Teratogenic
- **Clofazimine 300 mg**
  - Daily
  - Reduce Dose gradually to normal within 2 months to avoid Toxicity
- **Prednisone 300 mg**
  - initially
  - if Thalidomide is Contra

Type I

- **Prednisone** starting 50-80 mg/daily
  ↓
  gradually Reducing The Dose specially in Sever Cases of Neuritis ? Iridocyclitis
  ↓
  ↓ with hourly Then 4 hourly =
  1% **Hydrocortisone** eye Drops
  +
  atropine 1%
  OR **Scopolamine 0.15%**

III Educate the ptn:

- to cope è anesthetic Hand or Foot
  (e.g) Daily inspection for warmth + Bruising
  Wearing gloves at work, Avoid Burning heat

IV ↓ of complication of Nerve Damage:

→ **Anesthesia**: well-fitting shoe (specially if prescence of Deformity)
→ **Rest** → if injury or ulcer
→ **Physiotherapy**: weakness or paralysis

V Prevention + Control:

1. Health eduction
2. Early Case Detection
3. Early ↓ è Chemotherapy "MDT"
4. Child Contacts of lepromatous Cases:-
   Benfit from prophylactic chemotherapy 6 months (pauci)
5. Vaccination:
   → BCG (Cultivable mycobacterium)
   → killed M. leprae Isolated from experimentaly armadillos
   → killed M. leprae + BCG
   → Recombinant vaccine By genetic engineering of DNA

	Erythema nodosum	Erythema induratum of Bazin
CP	- The most common cause of panniculitis (septal panniculitis without vasculitis) - Multiple, bilateral, symmetrical, tender, warm, red nodules on shins of tibia, may be on thigh or forearm - Spontaneous healing with bruise-like appearance without ulceration or scarring - Acute course , recurrent - Fever, malaise, arthralgia, leukocytosis	- Usually affects women who have TB - Tender, nodules on the back of lower legs, calves - It may ulcerate → irregular, shallow, bluish undermined edge ulcer, healing with atrophic scar - Persistent or recurrent
Pathogenesis	- Reactive erythema to many etiological factors: streptococcal infection, drugs, sarcoidosis, TB - May be due to immune complex	- It may be tuberculid - Past or active foci of TB may be present
HP	- Deep skin biopsy - Septal inflammatory infiltrate - Septal vascular endothelial swelling - Edema & hge - Predominance of lymphocytes, histiocytes & giant cells - No leukocytoclastic vasculitis - No fat necrosis	- Epitheliod cell tubercles in deep dermis - Proliferation of walls of blood vessels & inflammatory infiltrate (vasculitis) → endothelial swelling + thrombosis → occlusion & necrosis
ttt	1- The cause 2- Bed rest 3- NSAID 4- K iodide	1- AntiTB 2- Dapsone 3- Systemic steroid

	Scrofuloderma	Lichen scrofulosorum
Etiology	Direct extension to the skin from underlying tuberculous focus, LN, bone, joint, epididymis	Hematogenous dissemination of tubercle bacilli from a distant source → delayed type hypersensitivity response **Tuberculid**
Tuberculin test	+ve	+ve
bacilli	Present in the lesion	Absent in the lesion
CP	Bluish red, nodule → ulcer with bluish undermined edges & floor covered with soft granulation tissue, sinuses & fistulae may present ,	Bilateral, symmetrical, grouped, closely set, minute lichenoid, slightly scaly, reddish brown, perifollicular papules, trunk
Healing	scarring → irregular adherent masses, puckered scarring	Without scarring
HP	Tuberculous granulation tissue with caseation necrosis in deeper tissue, bacilli may be found	Superficial dermal granuloma surrounds follicles & sweat ducts composed of epithelioid cells with some langhans giant cells & a narrow margin of lymphoid cells at the periphery, no caseation
ttt	Antituberculous drugs	

* ESR >100

1- TB
2. collagen Disease
3 - Malignancy

* Asteroid Bodies:

1- TB
2. Leprosy
3 - Sarcoidosis

* Diseased Caused By Cat:

1- Mycobacterial : TB
2- Backrial : Cat scratch D
- Cellulitis
3 - parasite : Scabies
4 - fungal : Dematophytes
5- atopic Dermatitis -
6 Urticaria

* Cicatricial alopecia:

* infections:
- MycoBact : LV- Leprosy
- fungal : Kerion - favus
- Protozoa : leishmaniasis
* congenital : eg : Dariers D
* Tramatic : Trauma, Burn
* Tumor : BCC, SCC.

* Hypopigmented macules on trunk:

1- Tuberculoid leprosy
2- morphea
3 - Vitiligo
4 - syphilis
5 - pityriasis alba
6 - Nevus Depigmentosus
7 - Tinea versicolor

* loss of outer one-third of eyeBrow:

1. Leprosy
2 - myxedema
3 - Trichotellomania
4 - alopecia areata

* Leonine face:

1 - Leprosy (LL)
2 - lesimaniasis
3 - Sarcoidosis
4 - Syslemic amyloidosis
5 - lipoid proteinosis
6 - Scleromyxedema
7 - lymphoma Cutis
8 - leukemia Cutis
9 - Nodular mastocytosis
10 - Histocytosis
11 - Actinic Dermatitis

Q Mycobacterial Infections:

1- Mention 3 diseases caused by M. tuberculosis.
2- Tuberculosis cutis.
3- Naked tubercle.
4- Orificial tuberculosis: DD, investigations, ttt.
5- Cutaneous tuberculosis: clinical varieties, pathology, management.
6- Tuberculosis verrucosa cutis.
7- Lupus vulgaris: histopathology, diagnosis & ttt.
8- Management of lupus vulgaris.

9- Classification &Clinical types of leprosy.
10- Clinical features of leprosy.
11- Spectrum of leprosy & diagnosis.
12- Borderline leprosy.
13- Clinical manifestations of paucibacillary leprosy.
14- Histopathology of leprosy.
15- Compare: histopathological features of tuberculoid leprosy & lepromatous leprosy.
16- Lepra reactions.
17- Compare: type 1 & 2 lepra reactions.
18- Investigations of lepramatous leprosy.
19- Lab investigation & ttt of multibacillary leprosy& lupus vulgaris.
20- Management & complications of lepramatous leprosy.
21- Diagnostic procedures of suspected case of leprosy.
22- WHO therapy of leprosy.
23- First line of systemic ttt of tuberculoid leprosy.
24- Treatment of leprosy.